Obesity in childhood and adolescence:

Growth paths, adiposity and metabolic signature

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Growth paths, adiposity and metabolic signature

Scope of the problem

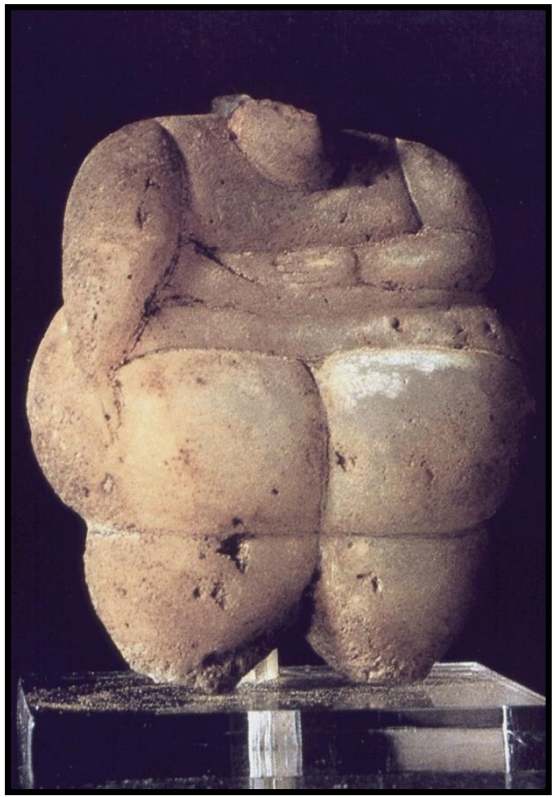
Social circumstances and molecular insights

Prevalence trends

BMI trajectories

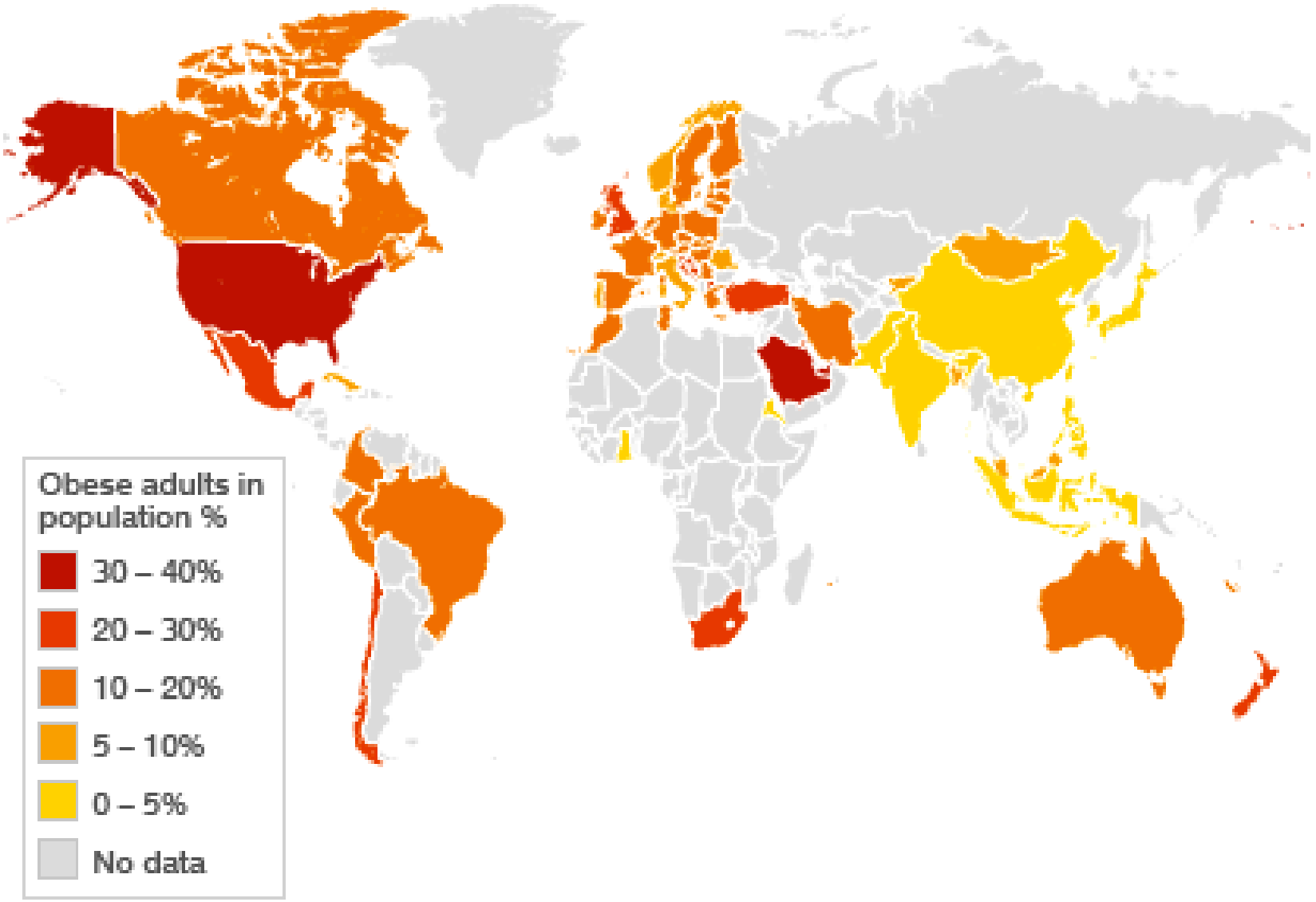
Conclusions and prevention

Growth paths, adiposity and metabolic signature



Scope of the problem

THE GLOBAL OBESITY PROBLEM



An obese adult is classified as having a Body Mass Index equal to or greater than 30

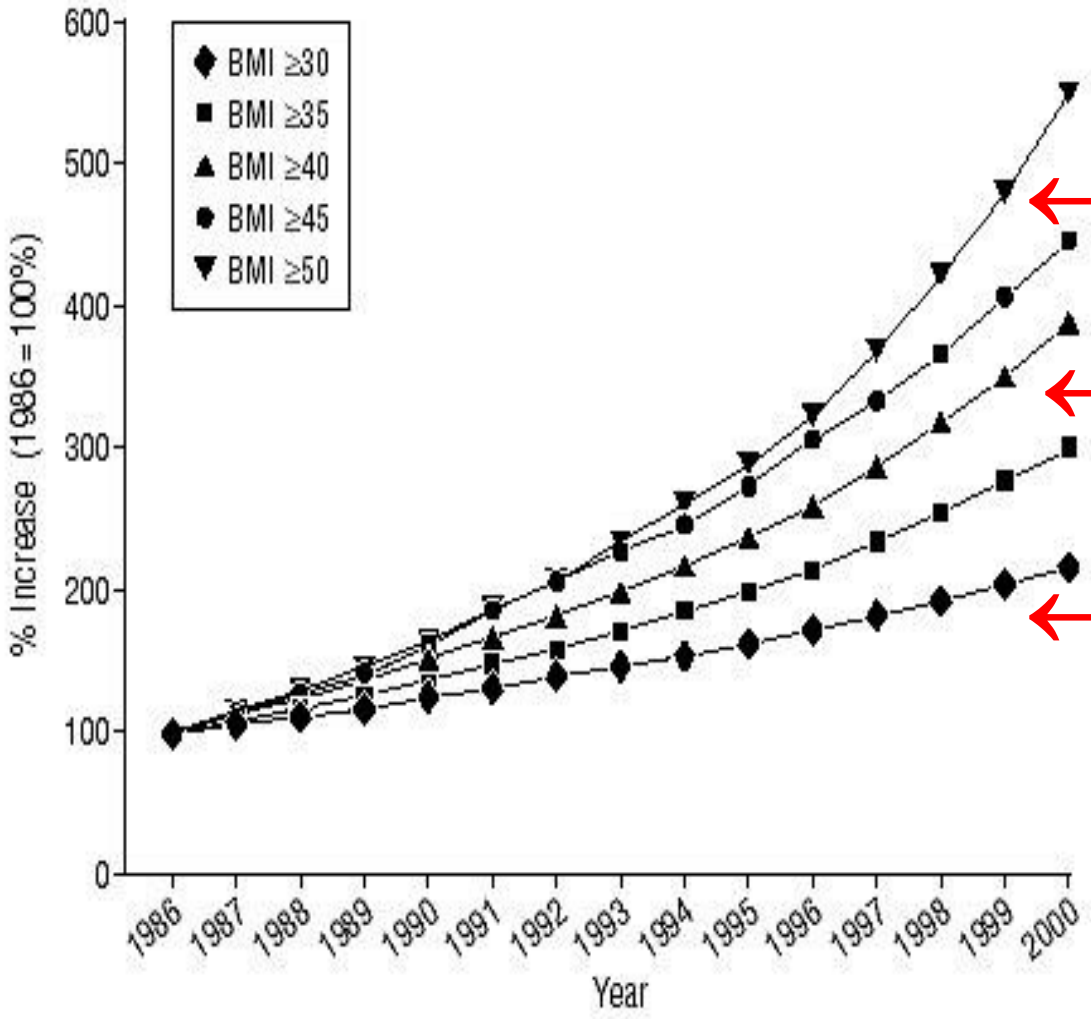
SOURCE: World Health Organization, 2005

Obese Chinese may top 200 million

BEIJING (AFP-Jiji) At least 200 million people in China will suffer from obesity within 10 years if current trends spurred by unhealthy lifestyles continue, state press said Saturday.

China currently has 90 million obese citizens whose weight is more than 20 percent in excess of their accepted level,

Increases in Clinically Severe Obesity, U.S. 1986-2000



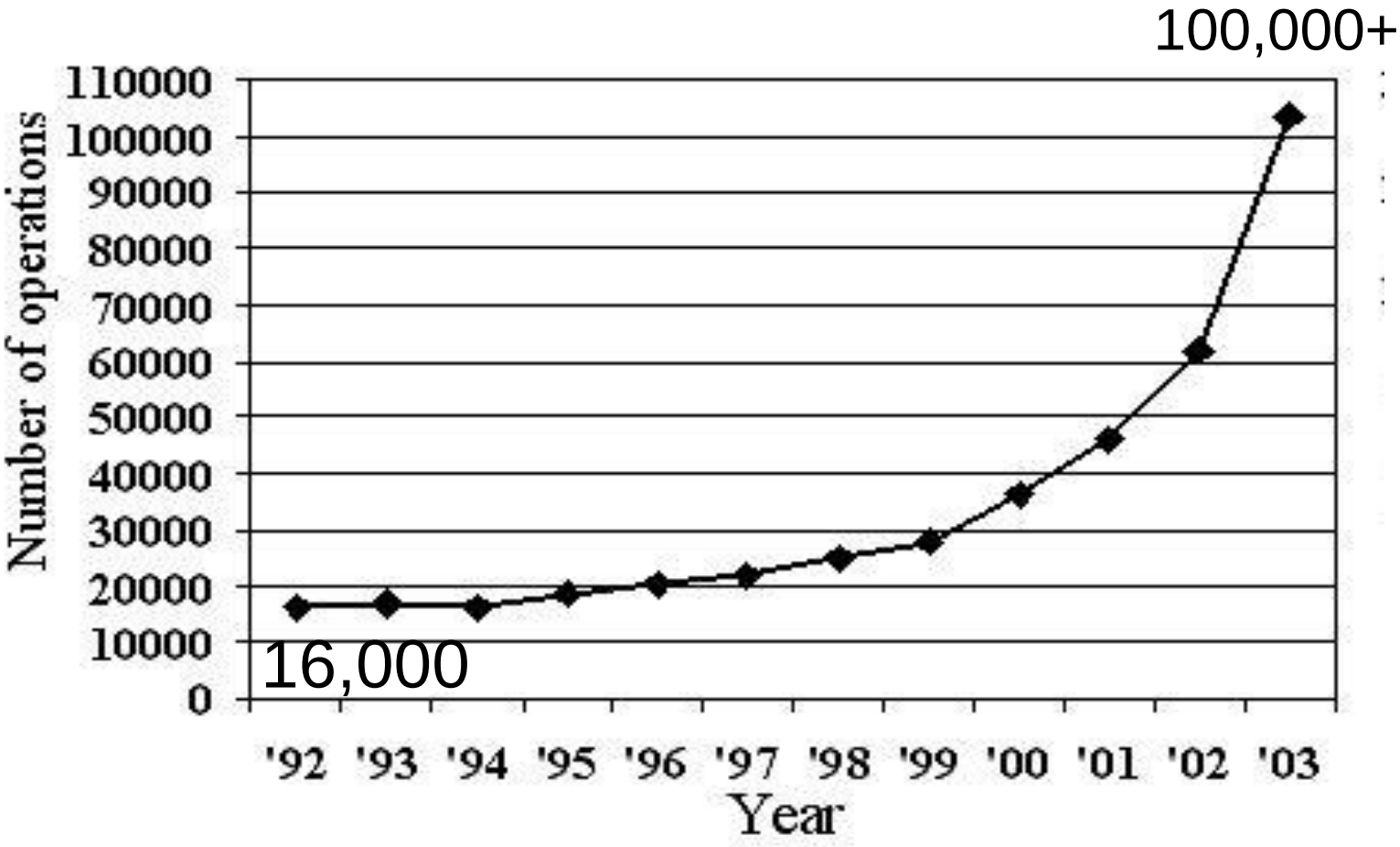
BMI ≥50 ↑ 5x
← 1/2000 to 1/400

BMI ≥40 ↑4x
← 1/200 to 1/50

BMI ≥30 ↑ 2x
← from 1/10 to 1/5

Sturm R. Arch Intern Med. 2003 Oct 13;163(18):2146-8

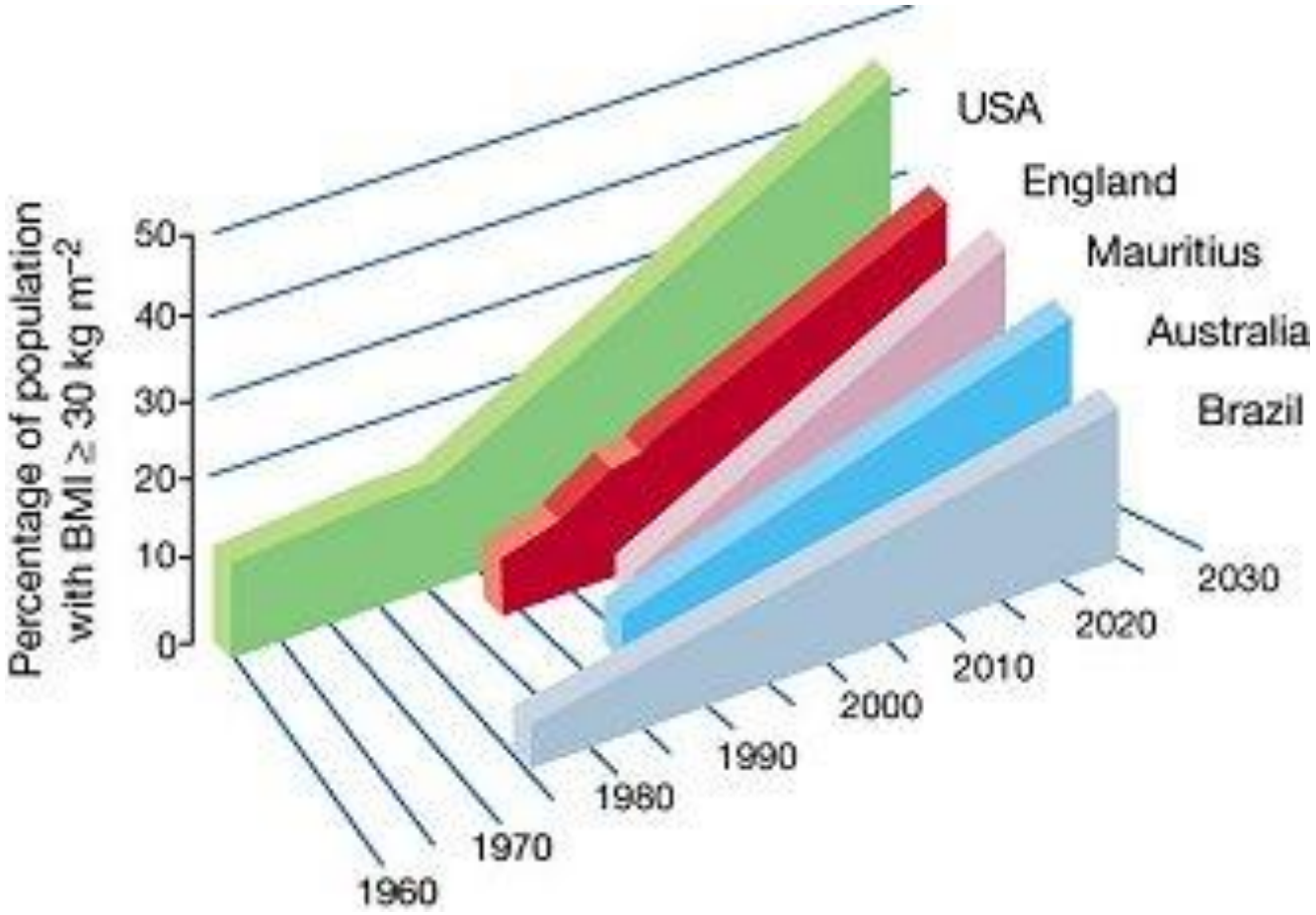
U.S. 1992 – 2003: Increased Demand for WLS



140,000 procedures anticipated for 2004

NEJM, 2004;350:1076

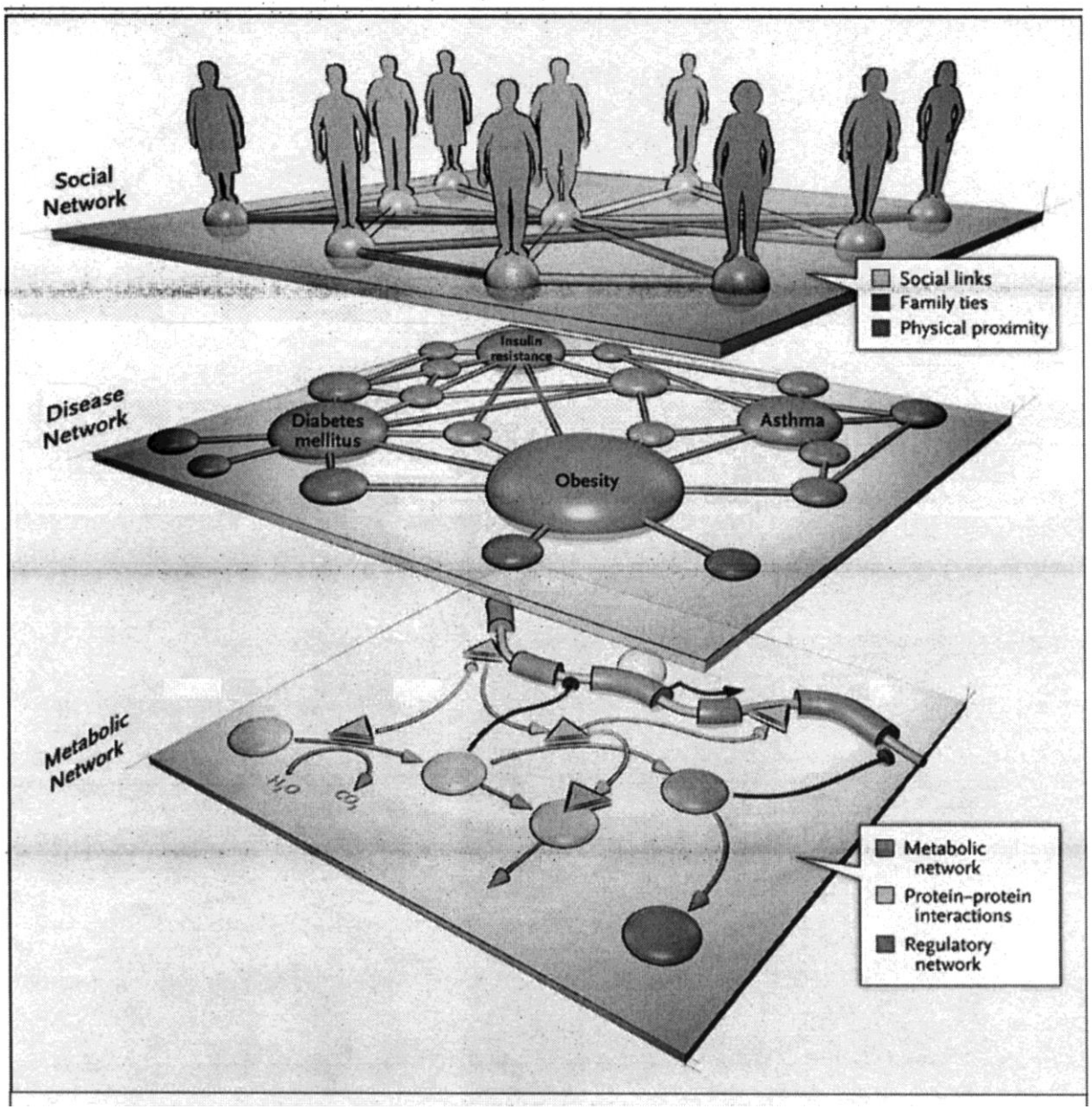
Obesity Rates: Projected to Double by 2030



Kuczmarski RJ et al. *JAMA*. 1994;272:205. Mokdad AH et al. *JAMA*. 1999;282:1519.
NIH Natl Heart, Lung, and Blood Inst. *Obes Res*. 1998;6(suppl 2):51S.

Growth paths, adiposity and metabolic signature

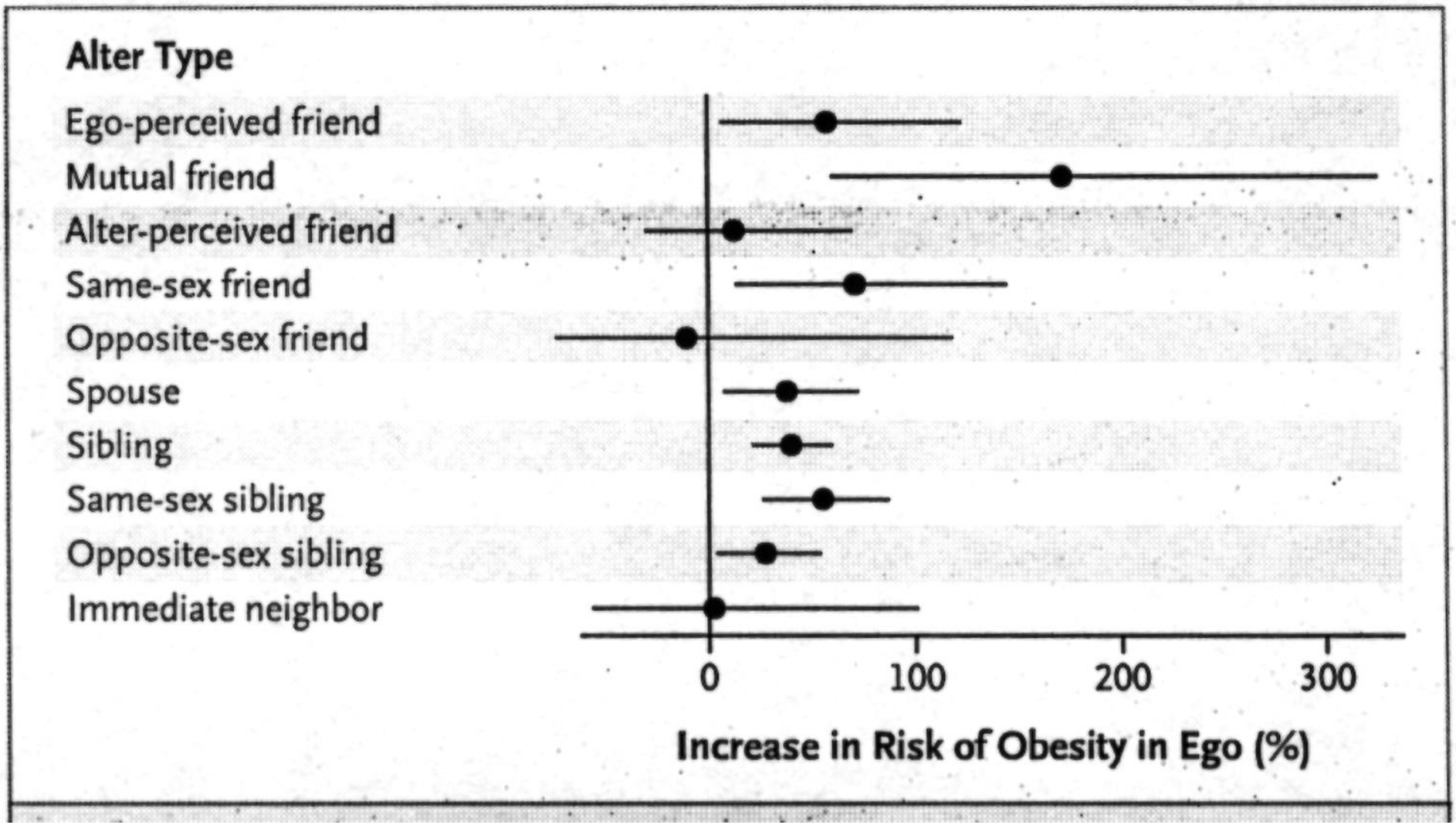
Social circumstances and molecular insights



(5) Christakis NA, Fowler JH

(6) Barabasi AL

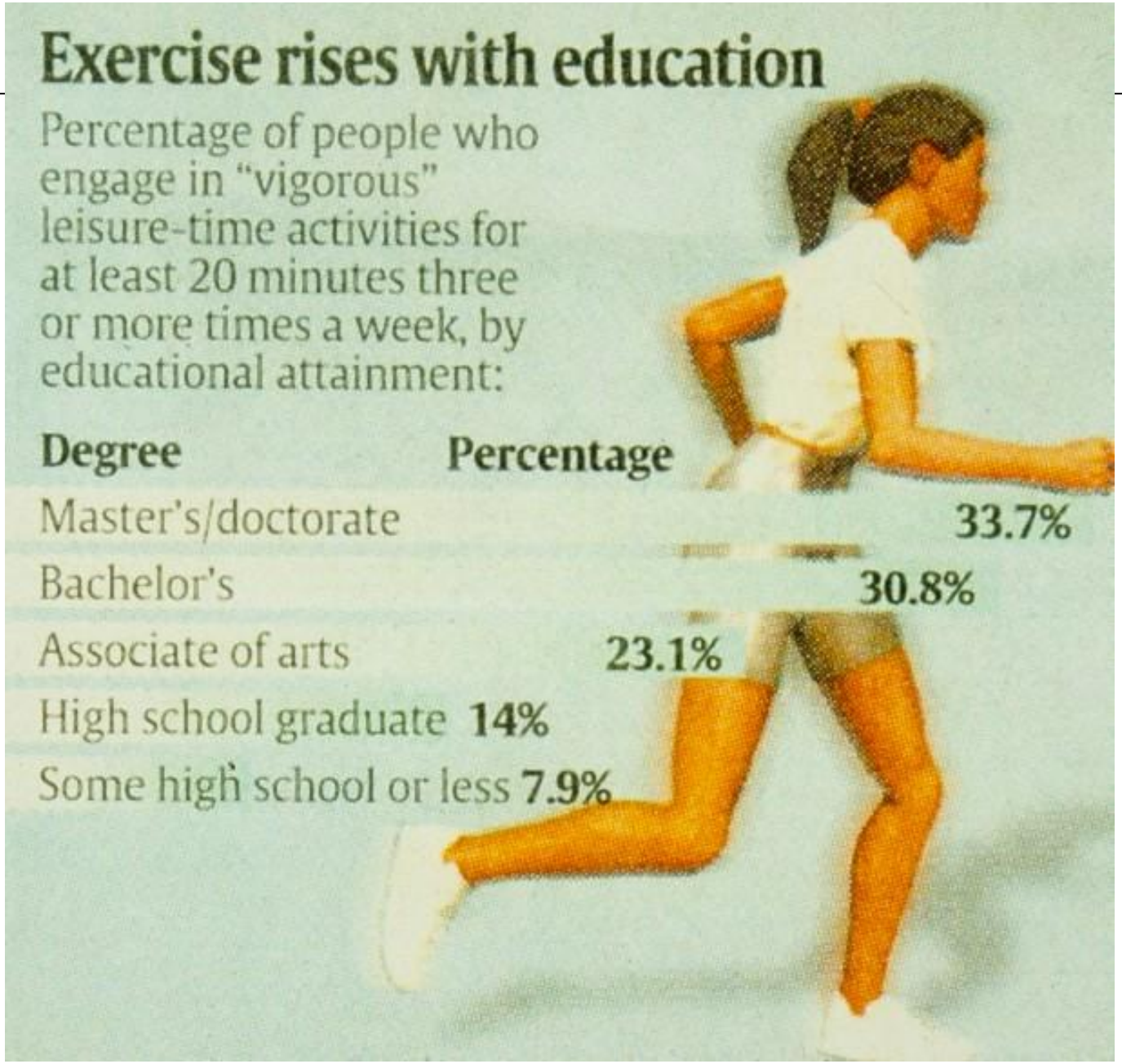
Social network of obesity orgins



Exercise rises with education

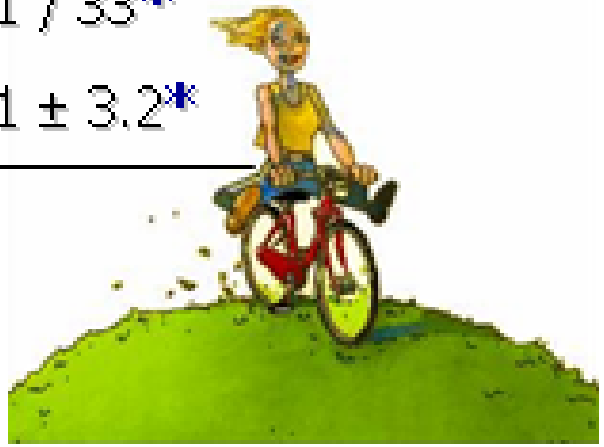
Percentage of people who engage in "vigorous" leisure-time activities for at least 20 minutes three or more times a week, by educational attainment:

Degree	Percentage
Master's/doctorate	33.7%
Bachelor's	30.8%
Associate of arts	23.1%
High school graduate	14%
Some high school or less	7.9%



Obesity: television and exercise

	obesity	normal w.
television (h/d)	3.9 ± 1.3	1.9 ± 1.0*
day (h/d)	1.2 ± 1.3	0.8 ± 0.7
evening (h/d)	1.2 ± 1.0	0.5 ± 0.6*
Sports club	11 / 32	21 / 33*
Sports (h/week)	1.1 ± 1.3	3.1 ± 3.2*

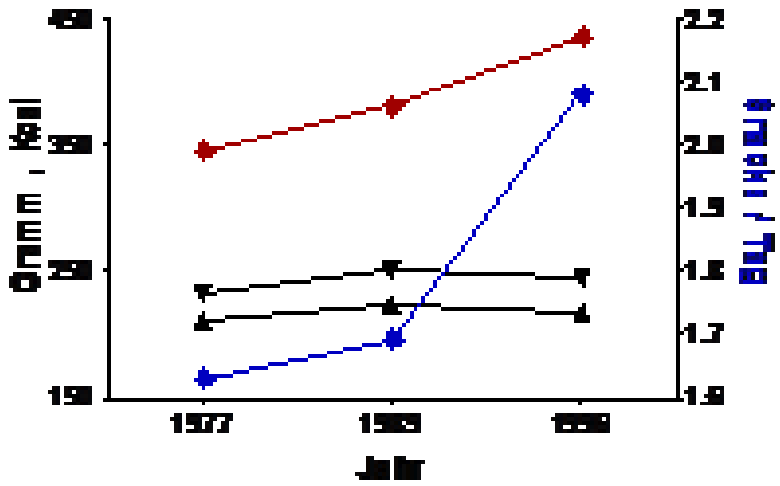


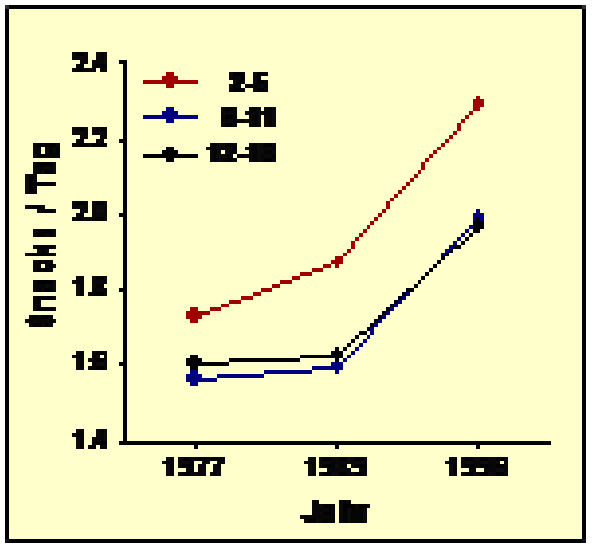
Dötsch J, Kinderarzt '97

Obesity and nutrition

	2 – 5 years			12 – 18 years		
	1977	*1989*	*1996*	*1977*	*1989*	*1996*
Snacks/day	1.73	1.87	2.29*	1.6	1.62	1.97*
Gram/Snack	158	167	153	275	298*	307
Kcal/Snack	171	187	175	296	320	318
Kcal/day	283	331*	378*	460	496	612*

Jahns L, J Pediatr '01





A 15-pound burger goes on sale

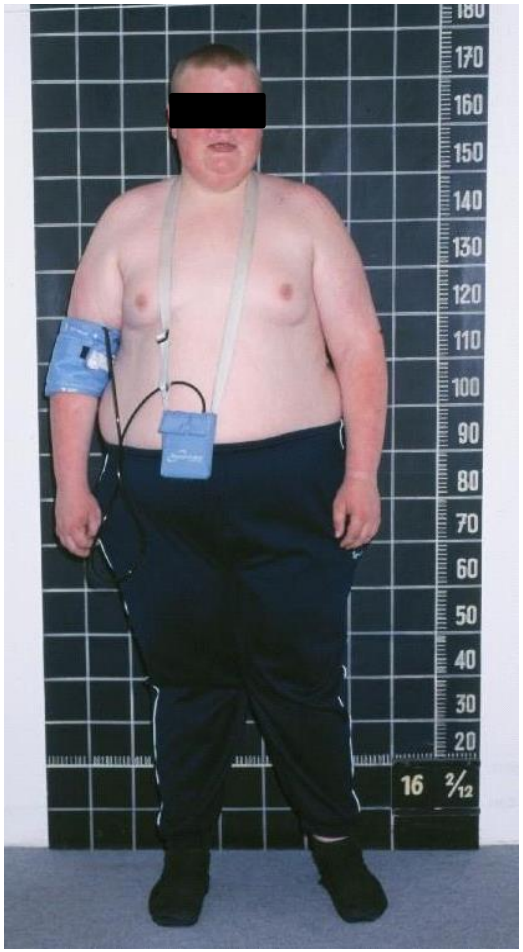
A Pennsylvania eatery is challenging diners to eat a huge burger at one sitting.

Obesity: nature and nurture

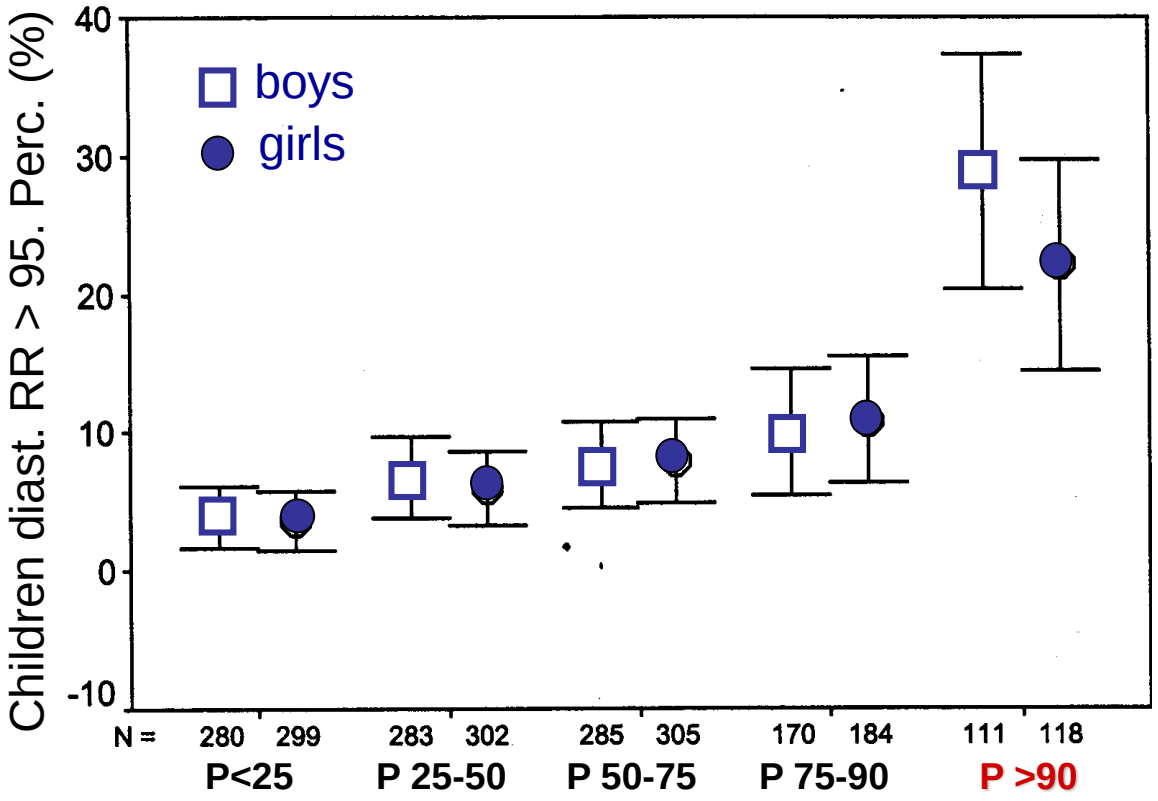
Consequences and co-morbidity

16 years old male
height: 176 cm
weight: 165 kg
BMI: 53 kg/m2

Type 2 diabetes
Hyperuricaemia
Hypercholesterinaemia
Elevated liver enzymes
fundus hypertonicus I°
„knee/joint aches“



Relation between obesity and blood pressure



Reich A et al, Int J Obes, 2003

Increase of hypertensive values with increasing BMI !

Etiology of obesity – *Contribution of genes ?*

Interaction of

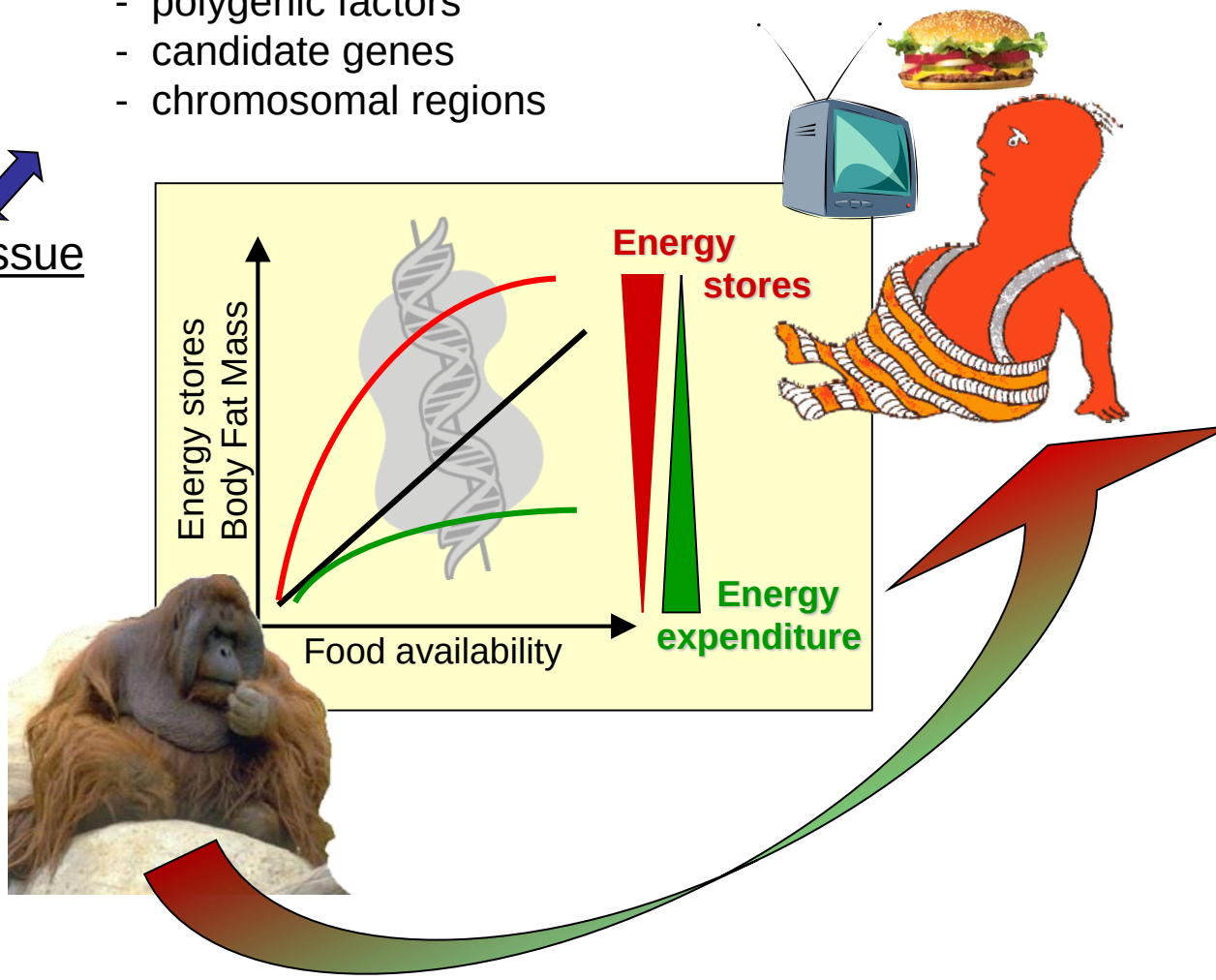
exogeneous factors

genetic factors

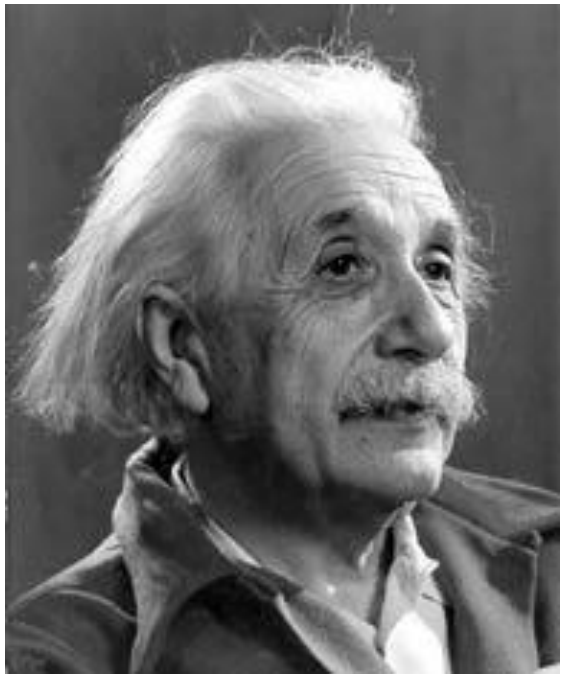
- polygenic factors
- candidate genes
- chromosomal regions

adipose tissue

- physical activity
- nutrition
- perinatal programming
- adiposity rebound
- **poverty**
- **lack of education**
- formula feeding
- television viewing

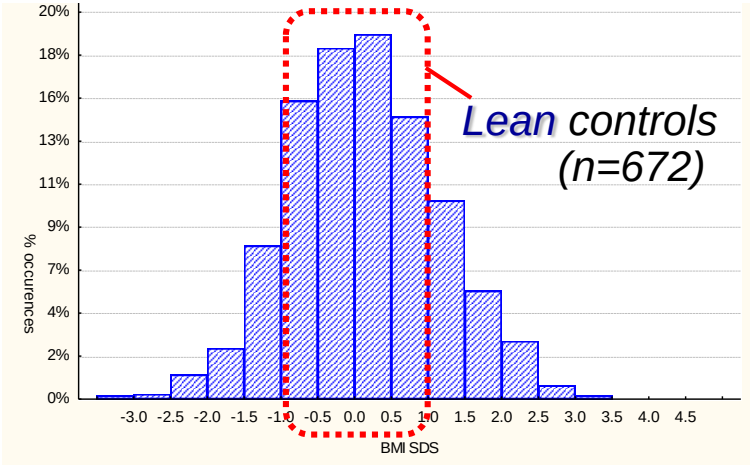


Human genetic diversity

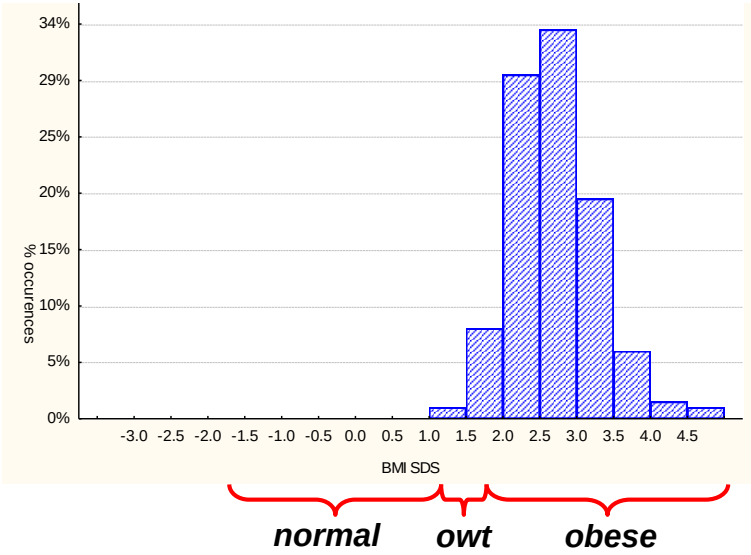


Genetic studies – *Cohorts and populations*

Leipzig Schoolchildren Project (n=1029)
→ Normal population



Leipzig Obesity Cohort (n=283)



Demographic characteristics of cohorts

	Normal	Obese	Lean
n	1029	283	672
Boys/Girls	488/541	146/137	353/319
Age (y)	11.6 ± 2.7	11.9 ± 3.8	11.7 ± 2.7
BMI SDS	0.11 ± 1.0	2.80 ± 0.6	-0.09 ± 0.5
Height SDS	0.15 ± 1.0	0.78 ± 1.2	0.03 ± 0.8

Genotyping Method:

- TaqMan Allelic Discrimination
- random selection of 10% re-genotyped
- all SNPs in Hardy-Weinberg-equilibrium

Clinical parameters in obesity cohort

- anthropometry
- blood pressure
- oral glucose tolerance test
- serum lipids
- liver enzymes

Genetic studies

Gene	Function	Approach	Association	
FASN	Enzyme fatty acid synthesis	candidate gene	↓ risk obesity ↑ beneficial lipid profile	*Körner A, et al.* *Int J Obes 2007*
PBEF	Enzyme NAD Metabolism	candidate gene	no ass. with obesity (↑ blood pressure)	*Körner A, et al.* *Metabolism 2007*
ENPP1	Insulin receptor adaptor protein	candidate gene	↑risk obesity (↑ blood glucose levels)	*Böttcher Y, et al.* *JCEM 2007*
TCF7L2	Transcription factor	GWA	↑ blood glucose levels	*Körner A, et al.* *JCEM 2007*
FTO	unknown (Enzyme ?)	GWA	↑ risk obesity (OR 1.7)	*Dina C, et al.* *Nat genet 2007*
PCSK1	Enzyme neuroendocrine cells	candidate gene	↑ risk obesity	*Benzinou M, et al.* *Nat genet 2008*

Körner A, Front Horm Res 2008

Genetics – *Genome wide associations scans*

ARTICLES

nature genetics

Stage 1: n≈30 000
Stage 2: n>59 000

Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity

Gudmar Thorleifsson[1,14], G Bragi Walters[1,14], Daniel F Gudbjartsson[1], Valgerdur Steinthorsdottir[1], Patrick Sulem[1], Anna Helgadottir[1], Unnur Styrkarsdottir[1], Solveig Gretarsdottir[1], Steinunn Thorlacius[1], Ingileif Jonsdottir[1,2], Thorbjorg Jonsdottir[1], Elinborg J Olafsdottir[3], Gudridur H Olafsdottir[3], Thorvaldur Jonsson[2,4], Frosti Jonsson[1], Knut Borch-Johnsen[5,6], Torben Hansen[5], Gitte Andersen[5], Torben Jorgensen[7,8], Torsten Lauritzen[9], Katja K Aben[10], André LM Verbeek[11], Nel Roeleveld[11], Ellen Kampman[11], Lisa R Yanek[12], Lewis C Becker[12], Laufey Tryggvadottir[3], Thorunn Rafnar[1], Diane M Becker[12], Jeffrey Gulcher[1], Lambertus A Kiemeney[10,11,13], Oluf Pedersen[5,6,8], Augustine Kong[1], Unnur Thorsteinsdottir[1,2] & Kari Stefansson[1,2]

ARTICLES

nature genetics

Stage 1: n>32 000
Stage 2: n>59 000

Six new loci associated with body mass index highlight a neuronal influence on body weight regulation

*Cristen J Willer[1,77,78], Elizabeth K Speliotes[2,3,77,78], Ruth J F Loos[4,5,77,78], Shengxu Li[4,5,77,78], Cecilia M Lindgren[6,78], Iris M Heid[7,78], Sonja I Berndt[8], Amanda L Elliott[9,10], Anne U Jackson[1], Claudia Lamina[7], Guillaume Lettre[9,11], Noha Lim[12], Helen N Lyon[3,11], Steven A McCarroll[9,10], Konstantinos Papadakis[13], Lu Qi[14,15], Joshua C Randall[6], Rosa Maria Roccasecca[16], Serena Sanna[17], Paul Scheet[18], Michael N Weedon[19], Eleanor Wheeler[16], Jing Hua Zhao[4,5], Loonie C Jacobs[20]

BRIEF C

nature genetics

Stage 1: n= 1 380
Stage 2: n=14 186

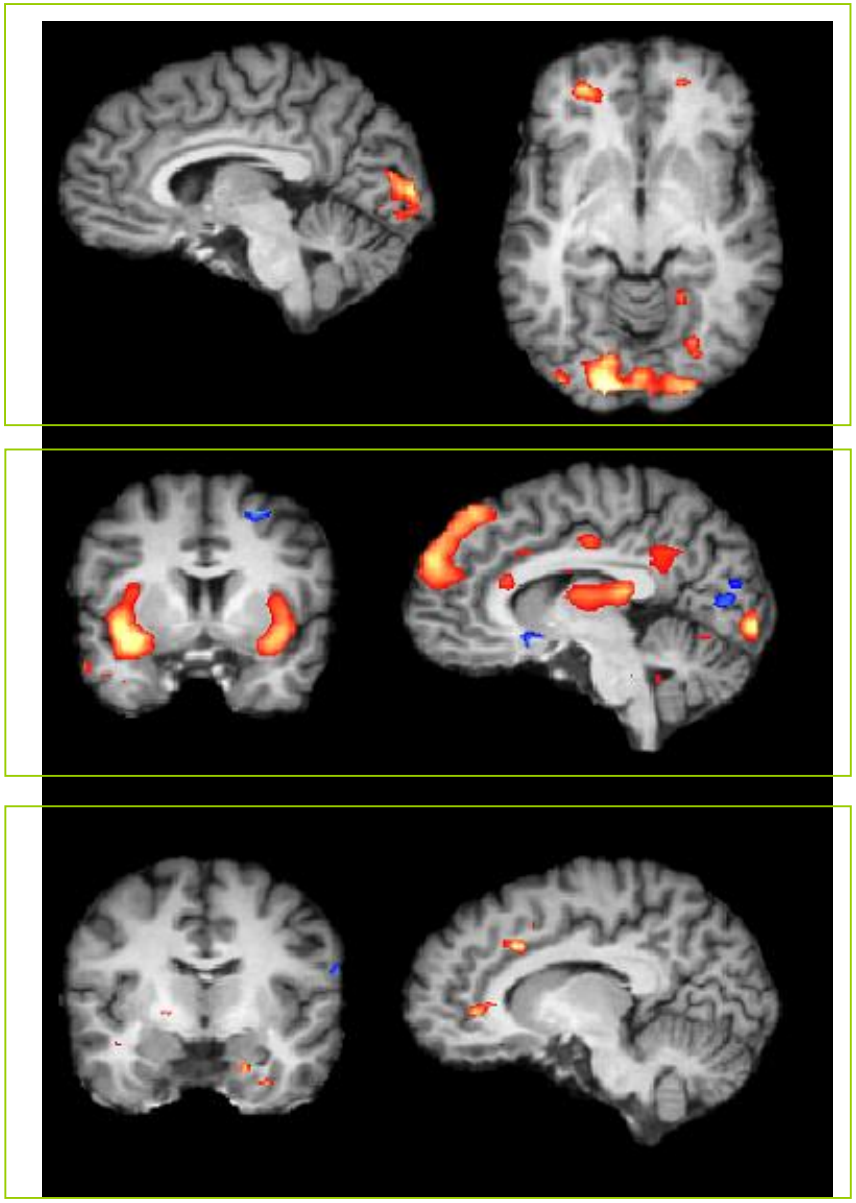
Genome-wide association study for early-onset and morbid adult obesity identifies three new risk loci in European populations

David Meyre[1], Jérôme Delplanque[1], Jean-Claude Chèvre[1], Cécile Lecoeur[1], Stéphane Lobbens[1], Sophie Gallina[1], Emmanuelle Durand[1], Vincent Vatin[1], Franck Degraeve[1], Christine Proença[1], Stefan Gaget[1], Antje Körner[2], Peter Kovacs[3], Wieland Kiess[2], Jean Tichet[4], Michel Marre[5], Anna-Liisa Hartikainen[6], Fritz Horber[7], Natascha Potoczna[7], Serge Hercberg[8], Claire Levy-Marchal[9], François Pattou[10], Barbara Heude[11], Maithé Tauber[12], Mark I McCarthy[13–15], Alexandra I F Blakemore[16], Alexandre Montpetit[17], Constantin Polychronakos[17], Jacques Weill[18], Lachlan J M Coin[19], Julian Asher[16], Paul Elliott[19], Marjo-Riitta Järvelin[19,20], Sophie Visvikis-Siest[21], Beverley Balkau[11], Rob Sladek[17], David Balding[19], Andrew Walley[16], Christian Dina[1] & Philippe Froguel[1,16]

MAX PLANCK INSTITUT FÜR KOGNITIONS- UND NEUROWISSENSCHAFTEN LEIPZIG

UNIVERSITÄT LEIPZIG

„Hunger Areas“



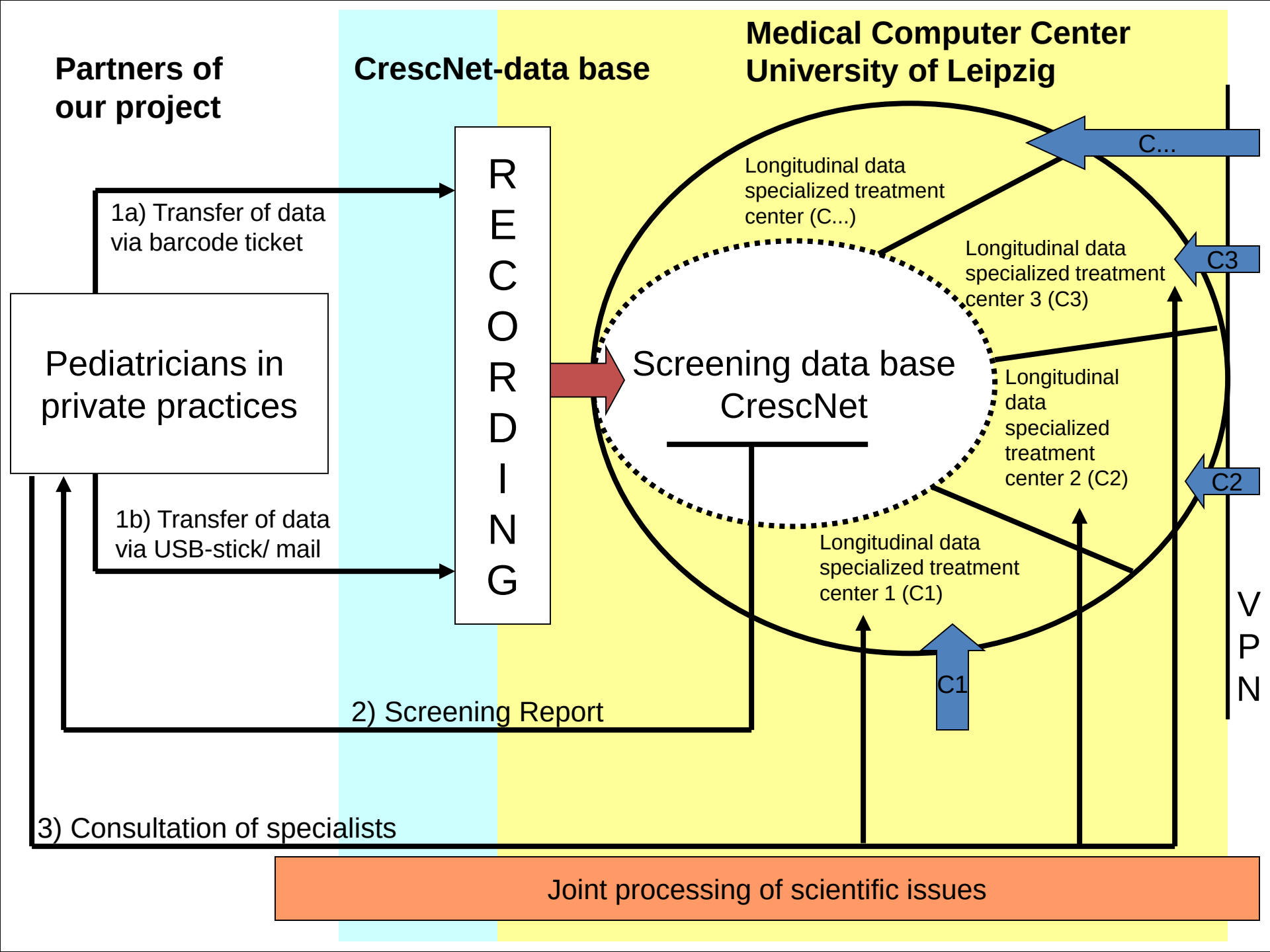
Führer et al. 2008
Obesity, in press

Obesity and overweight prevalence trends in Germany

Prevalence of obesity in the pediatric practice: results from the Crescnet data bank

Definitions - Crescnet

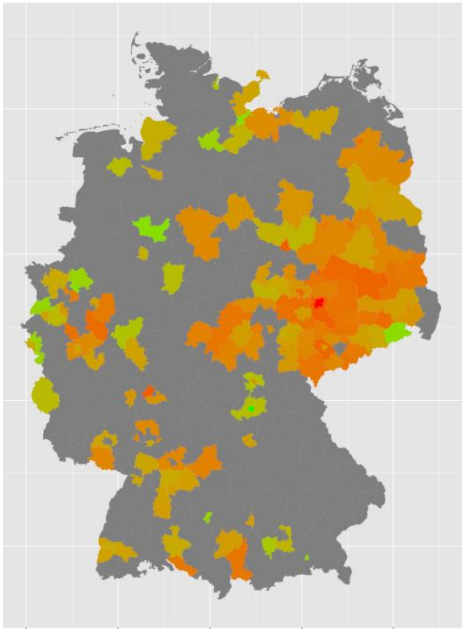
- Network of pediatricians and pediatric endocrinologists
- Public health instrument
- Research instrument

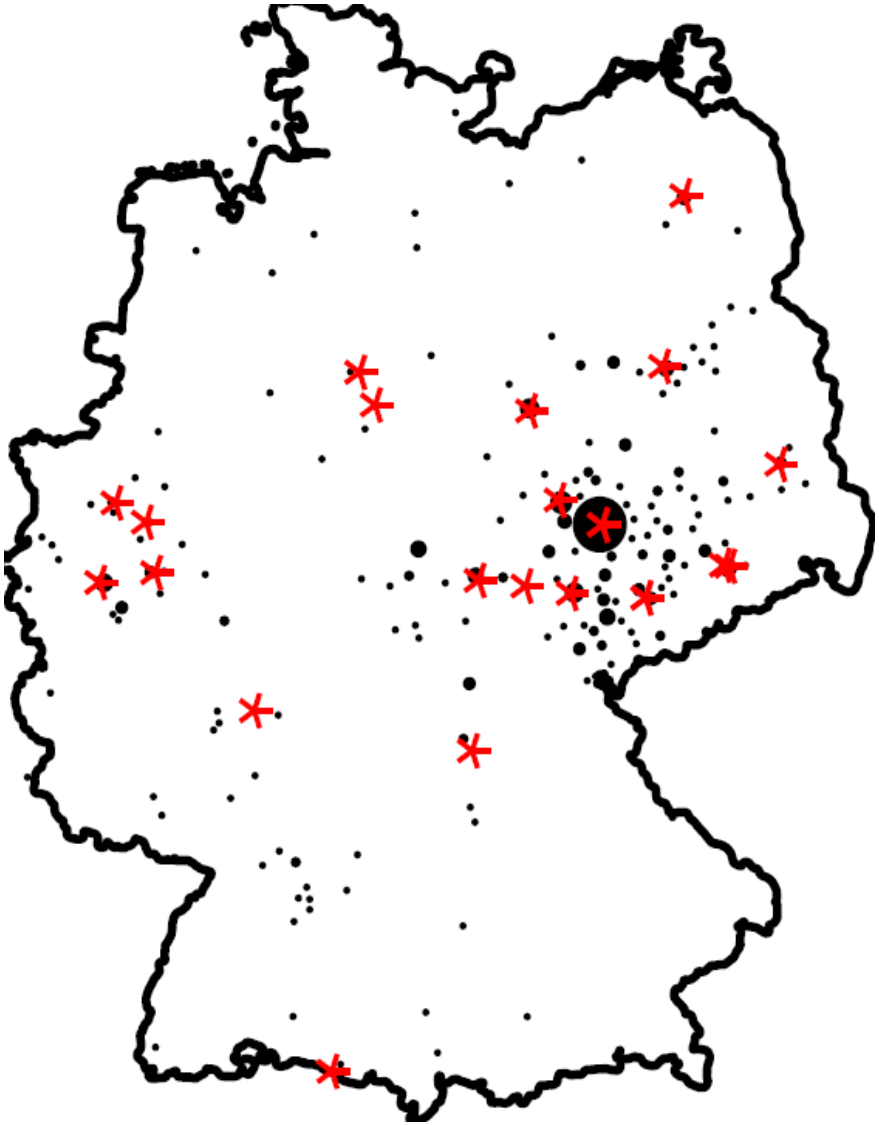

Partners of our project
CrescNet-data base
Medical Computer Center University of Leipzig
1a) Transfer of data via barcode ticket
Pediatricians in private practices
1b) Transfer of data via USB-stick/ mail
RECORDING
Screening data base CrescNet
Longitudinal data specialized treatment center (C...)
C...
Longitudinal data specialized treatment center 3 (C3)
C3
Longitudinal data specialized treatment center 2 (C2)
C2
Longitudinal data specialized treatment center 1 (C1)
C1
VPN
2) Screening Report
3) Consultation of specialists
Joint processing of scientific issues

Bridges to pediatric endocrinology

Universitätsklinikum Leipzig
Medizin ist unsere Berufung.

Links to and collaboration with pediatric endocrinology centers





Scientific evaluation
Example of a subgroup: pediatric endocrinology

864 patients (TxStart 2007-12)
Age at start of rhGH treatment

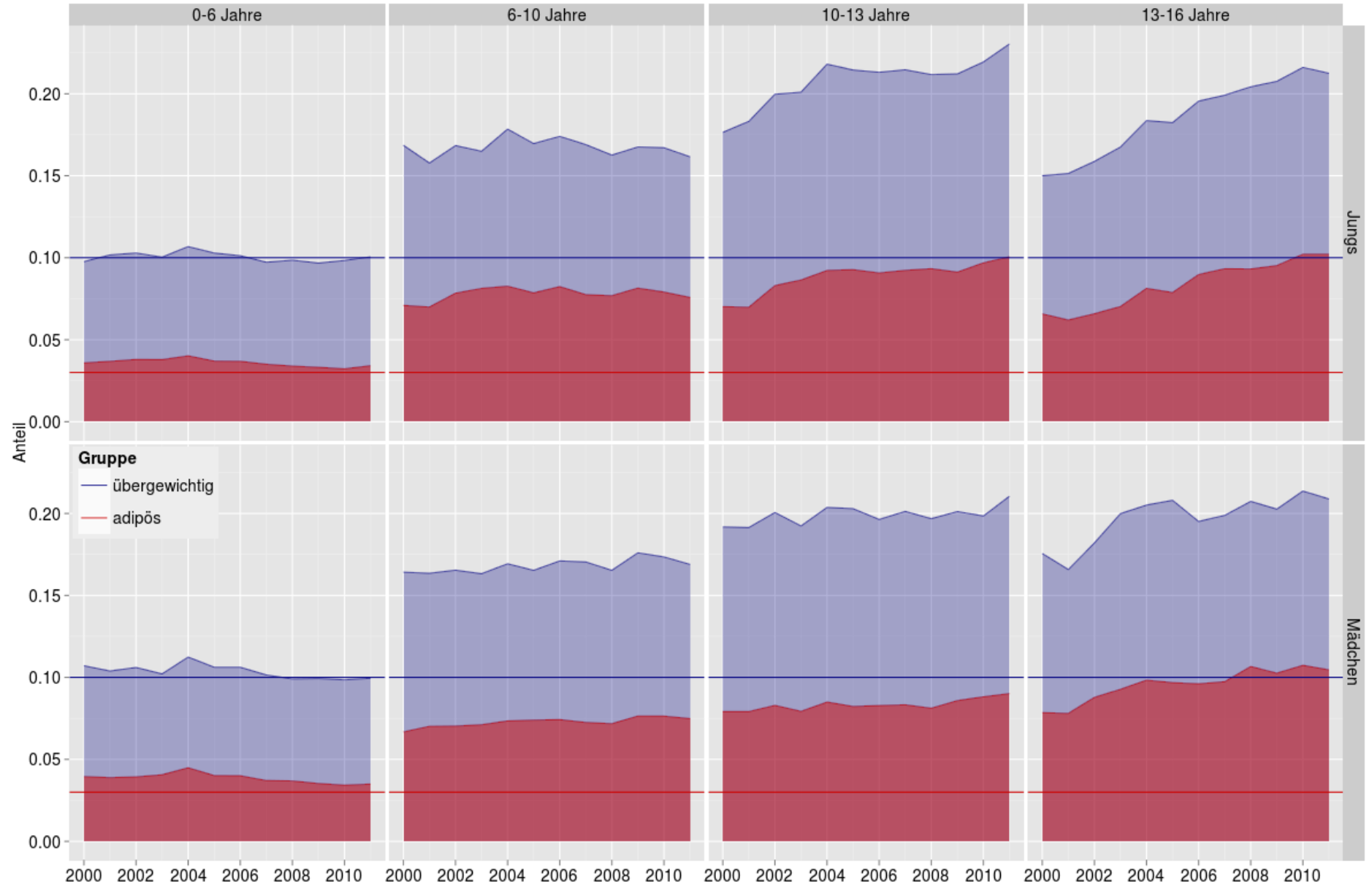
Calendar year	number	Age at start (mean)
2007	106	10,48
2008	131	8,89
2009	194	8,29
2010	207	8,42
2011	132	7,21
2012	94	7,02

Development of data bank Crescnet over time

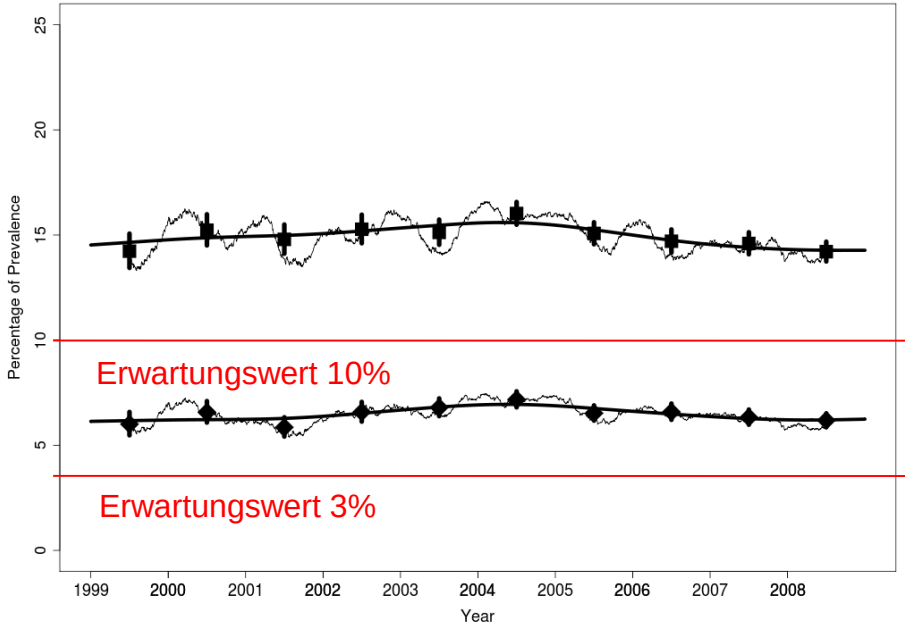
Date		practices	ped. endo.	children
Start	1998			
December	2000	132	5	93.863
December	2005	230	10	332.027
December	2010	304	24	523.663
August	2012	313	24	572.736*

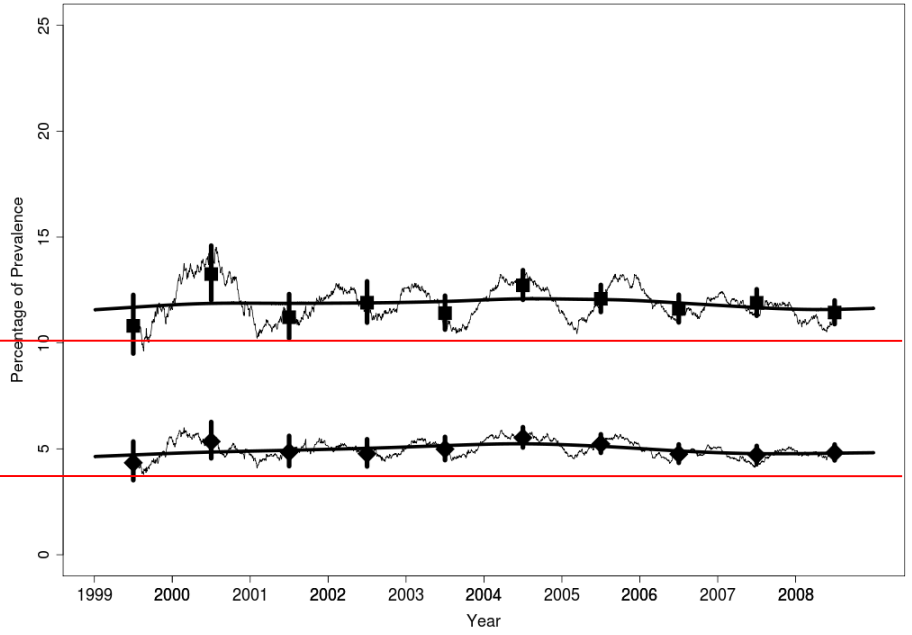
*with more than: 2.496.516 data entries

BMI - monitoring CrescNet 2000-2011



Prevalence of overweight (>P90) and obesity (>P97)
Trend analysis of CrescNet data in children
4-7.99 years of age





Boys

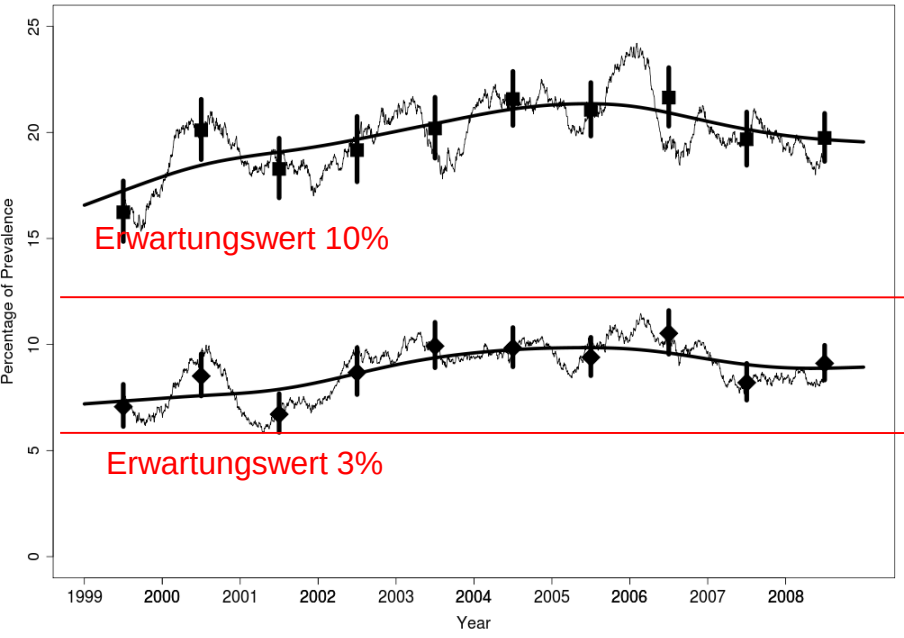
Girls

International Journal of Pediatric Obesity, 2010

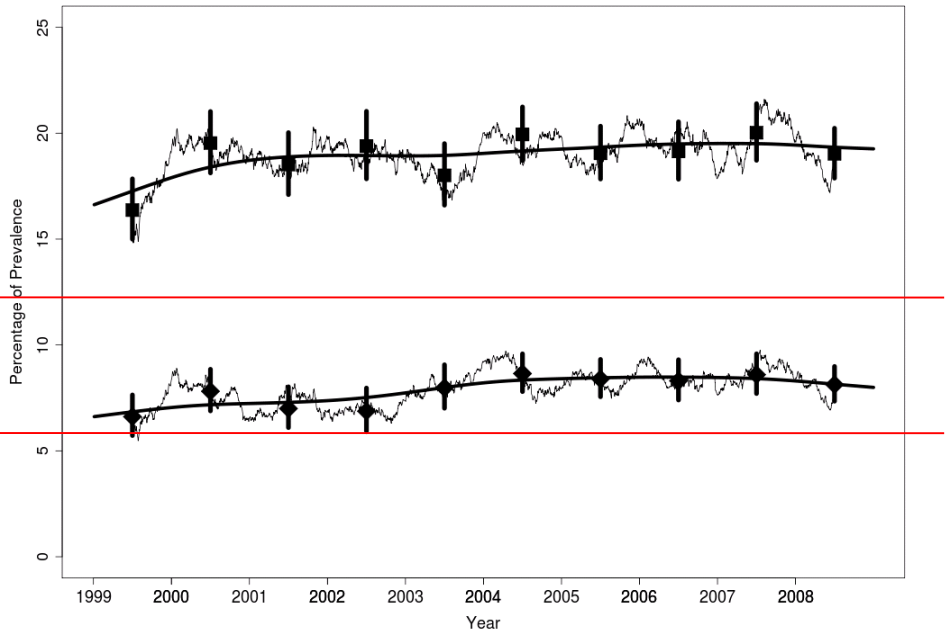
SUSANN BLÜHER, CHRISTOF MEIGEN, RUTH GAUSCHE, EBERHARD KELLER, ROLAND PFÄFFLE, MATTHEW SABIN, GEORGE WERTHER, RASHA ODEH & WIELAND KIESS

Age-specific stabilization in obesity prevalence in German children: A cross-sectional study from 1999 to 2008

Prevalence of overweight (>P90) and obesity (>P97)
Trend analysis of CrescNet data in children
8-11.99 years of age



Boys



Girls

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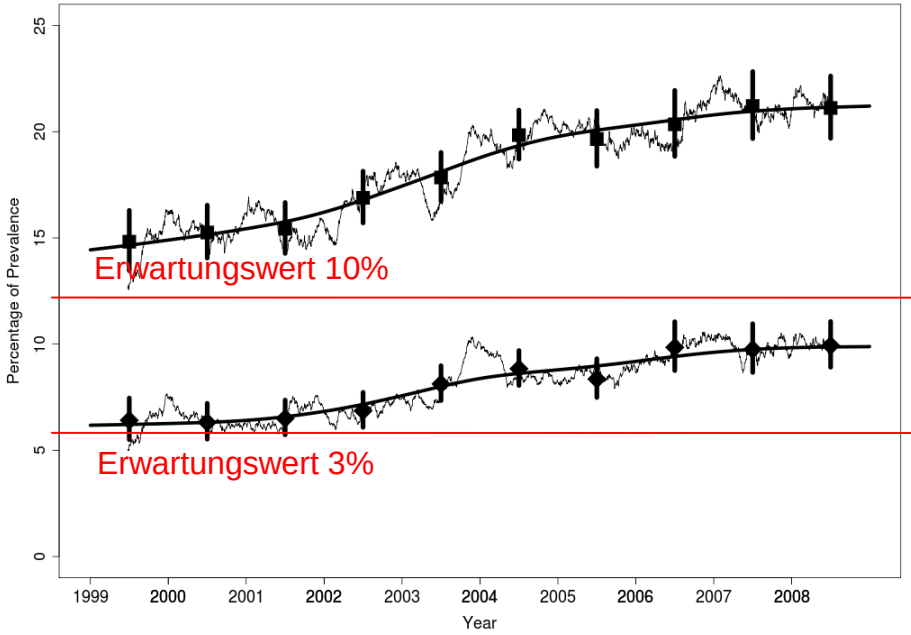
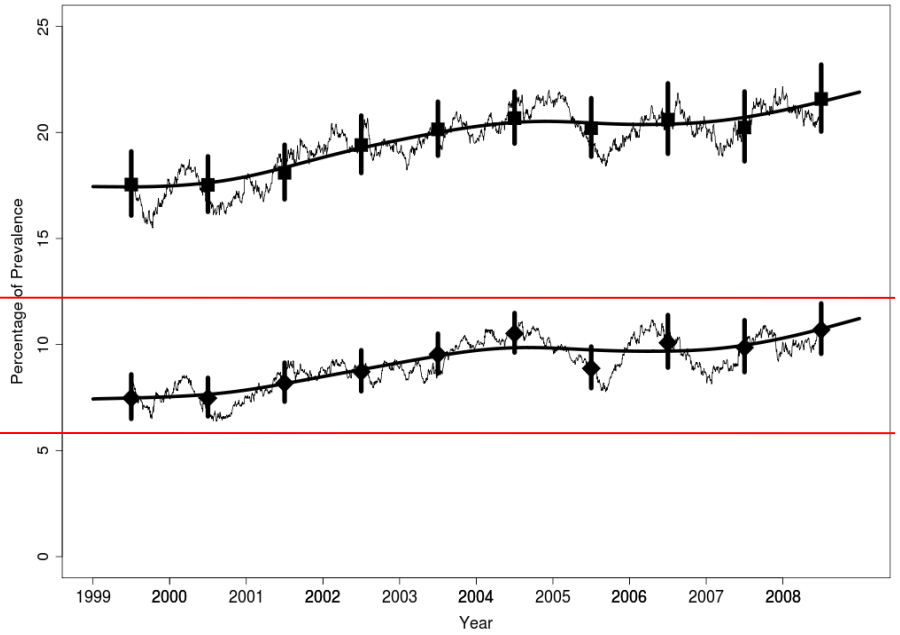
Age-specific stabilization in obesity prevalence in German children: A cross-sectional study from 1999 to 2008

Prevalence of overweight (>P90) and obesity (>P97) Trend analysis of CrescNet data in children

12-15.99 years of age



Boys



Girls

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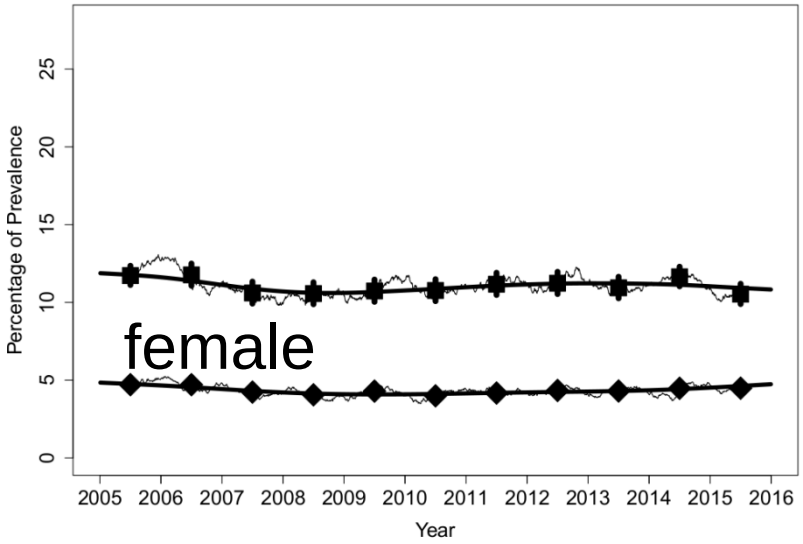
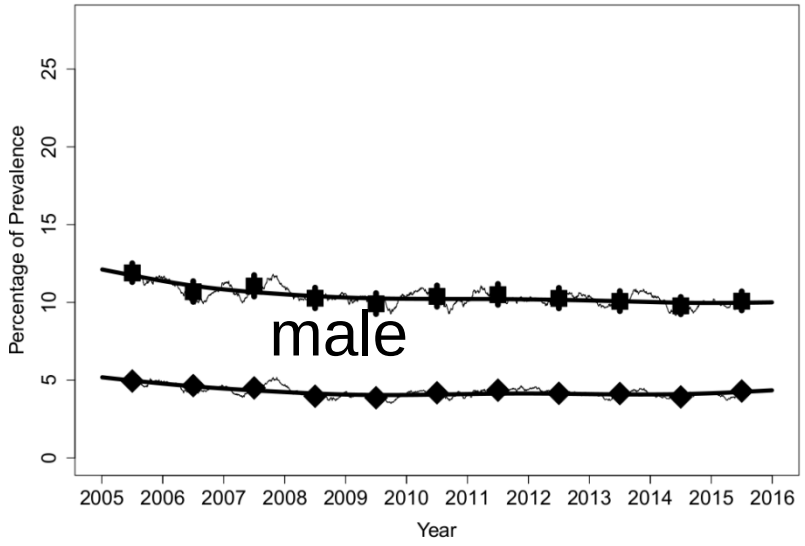
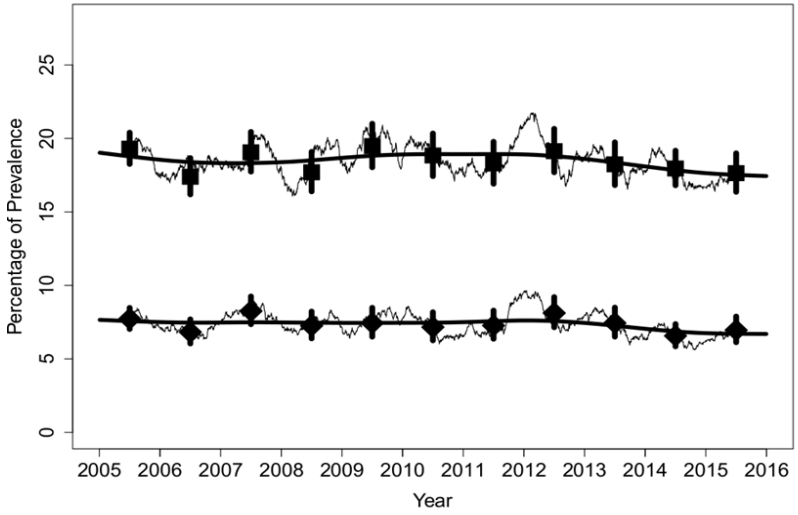
Age-specific stabilization in obesity prevalence in German children: A cross-sectional study from 1999 to 2008

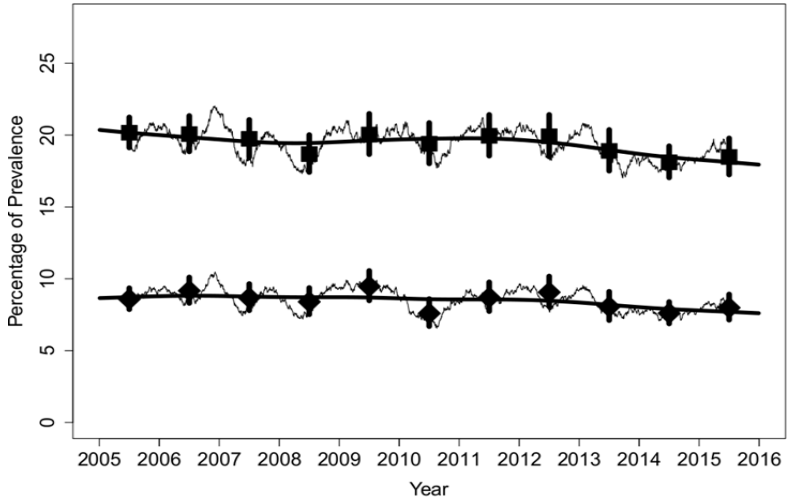
4-8 years old



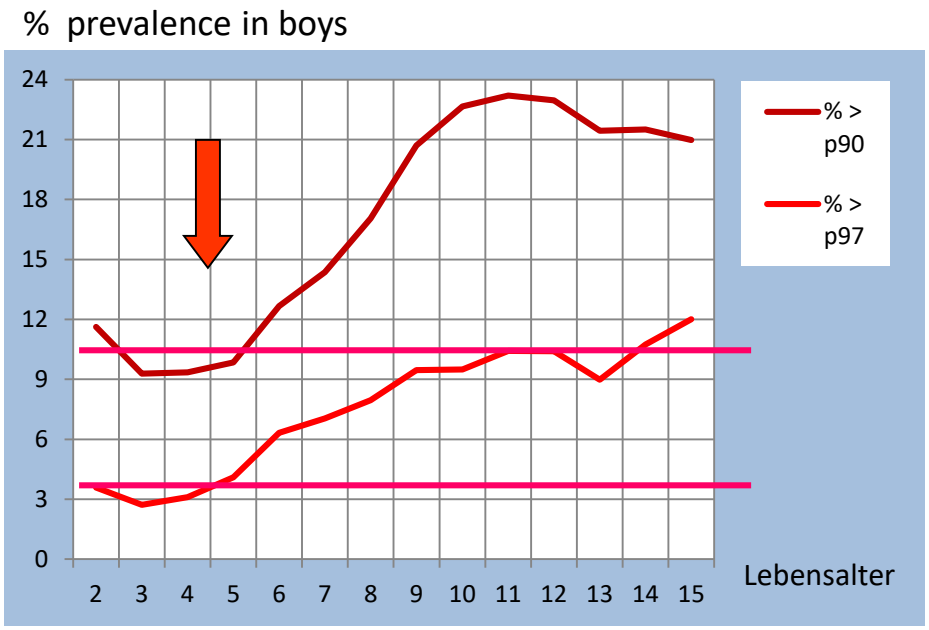


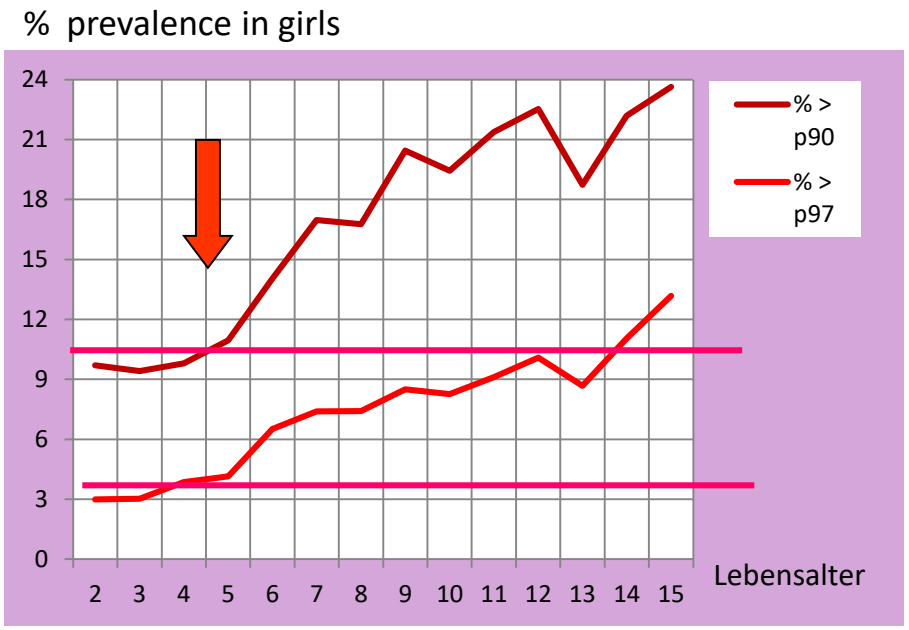
8-12 years old



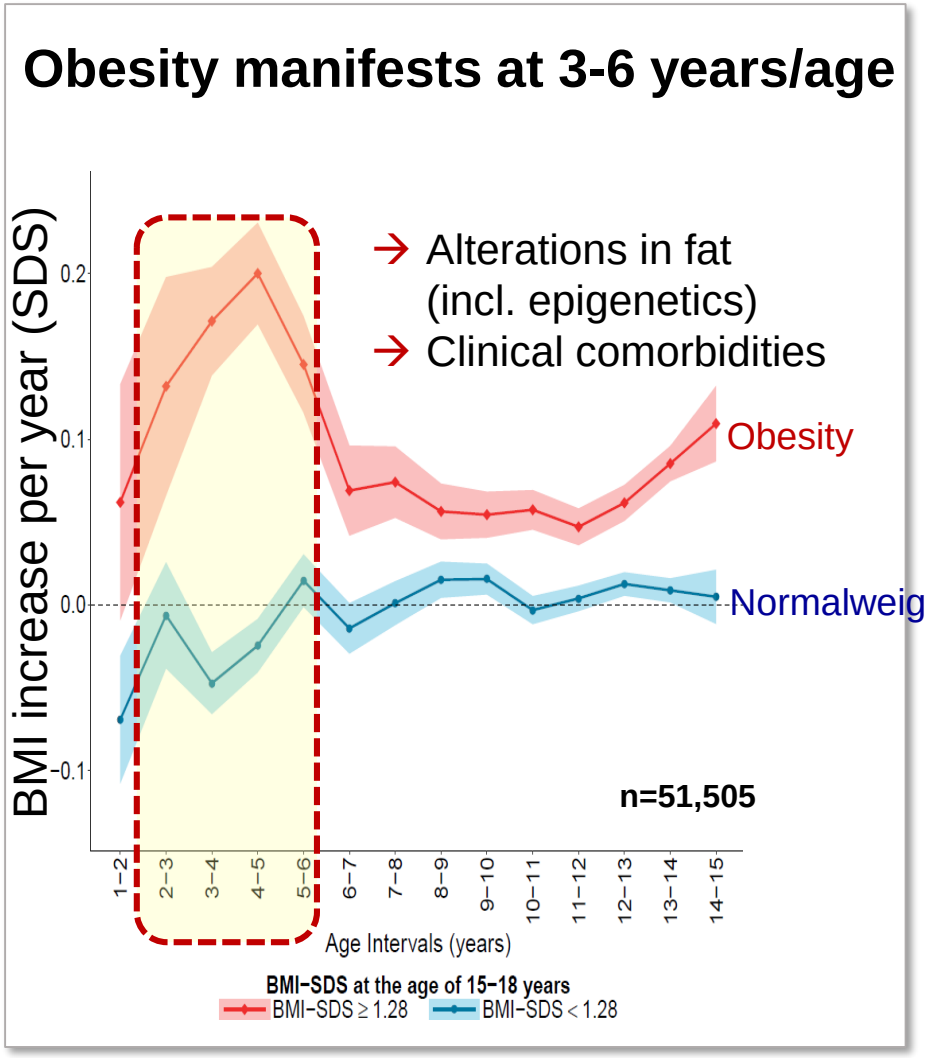


Prevalence rate for overweight and obesity
=> BMI trajectories





Reference: Kromeyer-Hauschild et al.



Growth paths, adiposity and weight trajectories

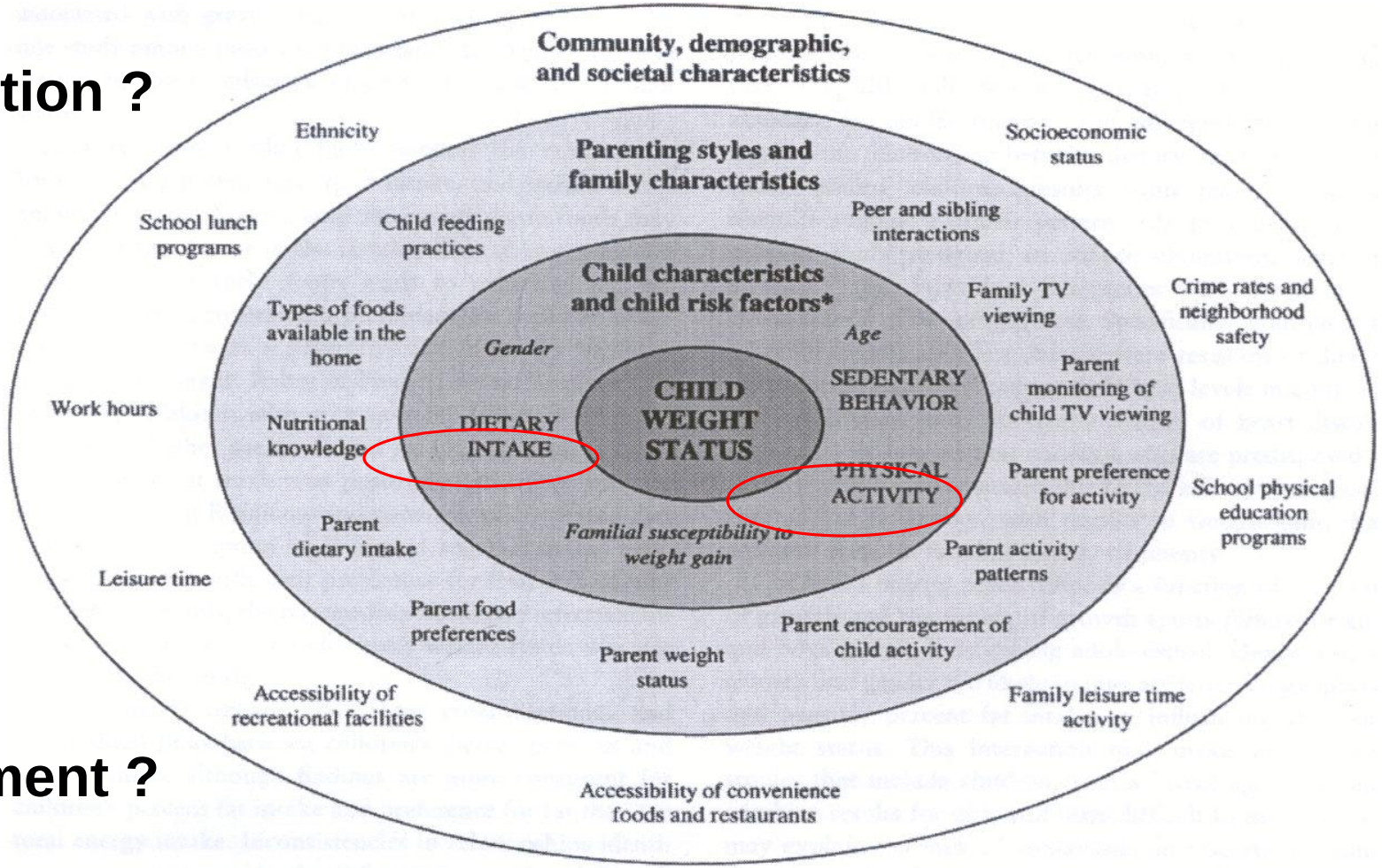
Geserick M, N Engl J Med 2018; 2019
Daalgard K, Cell 2016 164:353
Landgraf K, Diabetes 2015 64:1249
Mangner N, JACC Cardiovasc Imag 2014 7:1198

Growth paths, adiposity and metabolic signature

Conclusions and prevention

Causes of increase of overweight in children and adolescents

Prevention ?



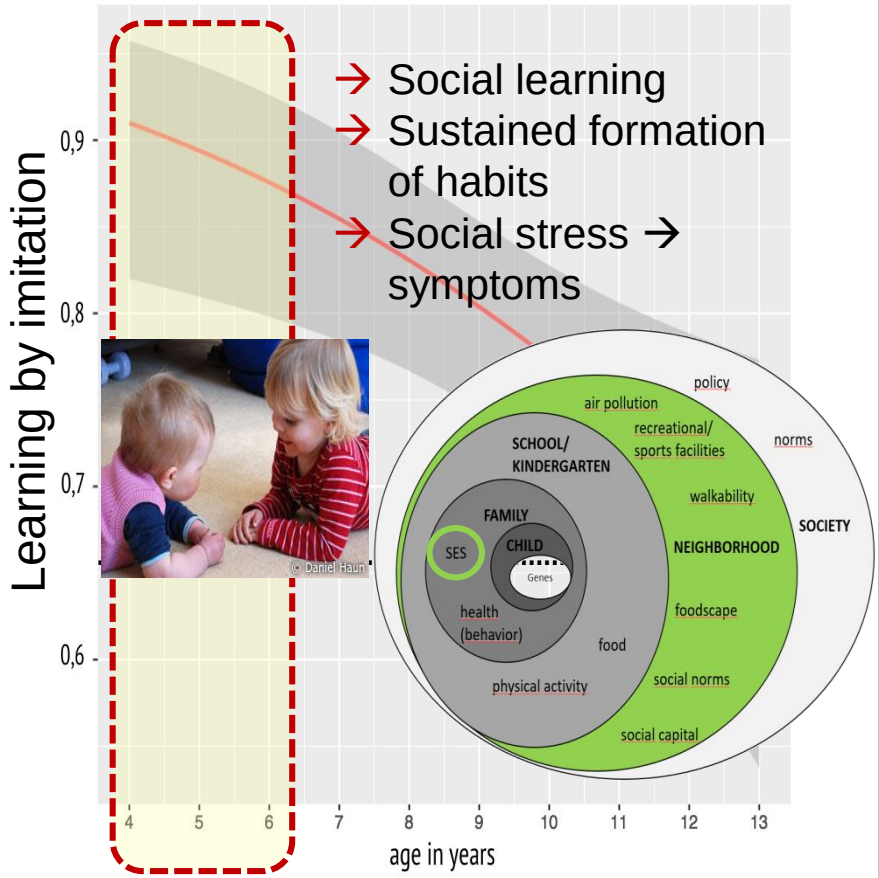
Treatment ?

Davison & Birch, 2001

Adiposity prevention, environment, conditions, and learning

Van Leeuwen EJC Nat Commun (*minor revision*)
Richter N PloS one 2016 11:e0145443
Lipek T J Ped Endocrinol Metab 2015; 28:485
Igel U Public Health 2016 139:209

Environment becomes influential



„Research Neighborhood“ – Health Ne

grünau bewegt sich
NETZWERK GESUNDHEIT

To develop successful preventive strategies:

- Start at the critical age
- Consider specific developmental mechanisms
- Address the risk population
- Target the living context

Understand how different obesogenic factors interact with individual predispositions

Intervention		Contrast
64%	Overweight/obesity	35%
12%	Childhood obesity	3%
12%	Unemployment	4%
48%	Welfare dependent	8%

→ Develop a biosocial obesity risk score

→ Identify protective factors

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IKK classic

KNAPPSCHAFT

Growth paths, adiposity and metabolic signature

Conclusion

Childhood obesity as a global, society problem

Thank you for your attention !